STEPS

New Drug Reviews

Saxagliptin (Onglyza) for Type 2 Diabetes Mellitus

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Am Fam Physician. 2010 Jun 15;81(12):1483-1484.

Saxagliptin (Onglyza) is the second oral dipeptidyl peptidaseï 4 (DPP-4) inhibitor to be marketed for the treatment of type 2 diabetes mellitus in adults. DPP-4 is the enzyme responsible for rapidly degrading incretin hormones released by the gut in response to meals.[1,2] The incretin hormones contribute to postmeal insulin secretion, as well as inhibit glucagon release, improve satiety, and slow gastric emptying. By inhibiting DPP-4, saxagliptin prolongs the glucose-lowering effects of the incretin hormones. Saxagliptin is labeled for use as monotherapy or in combination with metformin (Glucophage), sulfonylureas, or thiazolidinediones.[3]

Drug	*Starting dosage*	*Dose form*	*Approximate monthly cost**
Saxagliptin (Onglyza)	2.5 or 5.0 mg once daily; 2.5 mg in patients with moderate to severe renal dysfunction	2.5- and 5.0-mg tablets	$203

*ð *Estimated retail price of one month's treatment based on information obtained at http://www.drugstore.com/ (accessed May 18, 2010).*

SAFETY

Few adverse effects have been associated with saxagliptin. Unlike some other oral hypoglycemics, when saxagliptin is used alone it does not increase the likelihood of hypoglycemia.[1,3,4] When used as monotherapy or add-on therapy with metformin or thiazolidinediones, saxagliptin has an incidence of hypoglycemia that is comparable with placebo.[1,3,7] The manufacturer states that hypoglycemia is more common when saxagliptin is combined with glyburide (formerly Micronase), although the frequency is not significantly higher than with glyburide alone (13.3 to 14.6 percent versus 10.1 percent, respectively).[2,3] In 0.5 to 1.5 percent of patients, saxagliptin decreases lymphocyte count and causes lymphocytopenia (i.e., lymphocyte count of 750 cells per εL [0.75×10^9 per L] or less). Decreases in lymphocyte count have not caused any clinical sequelae; however, the effects of saxagliptin in patients with preexisting lymphocyte abnormalities (e.g., human immunodeficiency virus infection) are unknown.[3]

Patients with moderate to severe renal dysfunction (creatinine clearance of less than 50 mL per minute per 1.73 m^2 [0.83 mL per second per m^2]) require a dosage reduction to 2.5 mg once daily. The lower dosage also should be used in patients receiving strong cytochrome P450 3A4 and 3A5 inhibitors, such as clarithromycin (Biaxin), ketoconazole, and the antivirals ritonavir (Norvir), nelfinavir (Viracept), and atazanavir (Reyataz). Saxagliptin is U.S. Food and Drug Administration pregnancy category B.[3]

TOLERABILITY

Saxagliptin is well tolerated and produces bothersome adverse effects to a similar extent as placebo.[1,7] Saxagliptin does not seem to promote weight gain.[1,4,6] Up to 3.3 percent of patients will stop taking saxagliptin because of adverse effects. The rate of discontinuation is highest with the 5.0-mg dose, compared with the 2.5-mg dose (2.2 percent) or placebo (1.8 percent).[3]

EFFECTIVENESS

On average, saxagliptin monotherapy will lower the A1C level by 0.4 to 0.9 percent.[1,4] Adding saxagliptin to metformin, glyburide, or a thiazolidinedione will reduce the A1C level by an additional 0.6 to 0.9 percent.[2,6,7] Saxagliptin monotherapy will lower the average fasting glucose level by 9 to 22 mg per dL (0.50 to 1.22 mmol per L) and the postprandial glucose level by 24 to 45 mg per dL (1.33 to 2.50 mmol per L).[1,3,4] When used as add-on therapy, saxagliptin causes similar reductions in fasting and postprandial glucose levels.[2,6,7]

Efficacy trials with saxagliptin were no longer than six months in duration, and long-term studies of effectiveness and safety are currently ongoing. The effect of saxagliptin on diabetes-related morbidity and mortality, or all-cause mortality, is not known. Clinical trials have not investigated the combination of saxagliptin and insulin.

PRICE

A 30-day supply of the 2.5- or 5.0-mg tablets of saxagliptin costs approximately $203. A one-month supply of sitagliptin (Januvia), the other available DPP-4 inhibitor, costs $207 for the 100-mg tablets. As a comparison, the cost of metformin is $32 (brand: $141) for 60 (a one-month supply) of the 1,000-mg tablets.

SIMPLICITY

Saxagliptin is available in 2.5- and 5.0-mg tablets. Saxagliptin is taken once daily without regard to meals. There are no known contraindications to saxagliptin therapy.[3]

Bottom Line

Saxagliptin lowers A1C levels to a lesser extent and is much more expensive than first-line therapy with metformin. Its ability to decrease diabetes-related complications, including mortality, is not known. It is a DPP-4 inhibitor that has a more significant drug interaction profile than sitagliptin and offers little cost

advantage. For these reasons, saxagliptin should be reserved as an alternative therapy for patients who cannot tolerate other treatments for type 2 diabetes or in whom other treatments fail.

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Author disclosure: Nothing to disclose.

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